

Remarks

Claims 1-20 were pending. Claims 10, 11, 13 and 15 are cancelled without prejudice to prosecution in a future application, due to the restriction requirement. Claims 1 and 19 were cancelled as redundant. Claims 21-42 were added. Therefore, claims 2-9, 12, 16-18 and 20-42 are now pending

Amendments to the Claims

Claims 2-9, 12, and 16 were amended. Support for the new and amended claims can be found throughout the specification, for example:

Claims 2, 6, 7, 12: page 2, lines 6-7 and 19-21.

Claim 3: original claim 3.

Claims 4, 5, 9: amended for readability only.

Claim 8: original claim 8 and page 13, lines 22-25.

Claim 16: original claim 8.

Claims 21-32: original claim 3.

Claim 33: original claim 8.

Claim 34: page 17, lines 15-16.

Claims 35-36: page 4, lines 23-28.

Claim 37-38: original claim 3.

Claim 39: page 29, line 25- page 30, line 27.

Claims 40-42: page 32, line 20- page 34, line 21.

No amendments herein were made to distinguish prior art. Instead, the amendments were made to clarify the claims.

Summary of Telephone Interview

Applicants thank Examiner Kruse for the courtesy of a telephone interview with Applicants' representative Sheree Lynn Rybak, Ph.D. on May 12, 2004 and May 13, 2004. During this interview, the 35 U.S.C. §§112 and 103(a) rejections were discussed, as were declarations needed to overcome the rejections.

Applicants' representative explained that the invention is directed to transgenic plants that express dermaseptin peptides. In addition, Applicants' representative asserted that the claims should not be limited to particular dermaseptin peptides, because such peptides are well known in the art. Evidence for this position on page 7 of the application was noted to the Examiner. Applicants agreed to submit a §1.132 Declaration signed by Dr. Hancock, an expert in the field of antimicrobial peptides, explaining that those in the relevant art understand what a dermaseptin cationic peptide is. The Examiner noted that if the §112 rejections were overcome, the claims could be amended to rejoin the other dermaseptin molecules previously restricted out of the application (namely, SEQ ID NOS: 4-14).

In addition, Applicants' representative explained that the present invention was not obvious to the inventors because of the failures of others to obtain disease resistance in plants transfected with a cationic peptide. Applicants agreed to submit a §1.132 Declaration signed by co-inventor Dr. Misra, explaining why the invention was not obvious to her.

Applicants also agreed to cancel claim 1, and amend claim 2 to clarify that the plant has disease resistance.

Amendments to the Specification

A new abstract on a separate sheet is enclosed.

The specification has been amended to remove hyperlinks, remove redundancies, and to correct obvious typographical errors.

In view of these amendments, Applicants request that the objections to the specification be withdrawn.

Sequence Rules

The specification has been amended to include sequence identifiers for all amino acid sequences of four or more residues. In addition, a new sequence listing is enclosed that now includes SEQ ID NO: 42 (which was previously presented on page 4, line 27 of the specification).

In view of these amendments, Applicants request that the objections to the specification and sequence listing be withdrawn.

35 U.S.C. §112, second paragraph

Claims 1-9 and 19-20 were rejected under 35 U.S.C. §112, second paragraph on the ground that the phrase “a dermaseptin cationic peptide” does not teach the metes and bounds of the claimed invention. Applicants respectfully disagree and request reconsideration.

The phrase “a dermaseptin cationic peptide” teaches the metes and bounds of the claimed invention, because the specification provides a clear definition of dermaseptins, and those skilled in the art of antimicrobial peptides understand what the term “dermaseptin” means. The specification provides a clear explanation as to what is meant by the phrase “a dermaseptin cationic peptide” starting on page 6 line 29. Furthermore, numerous dermaseptin sequences are known, and are provided in the sequence listing (SEQ ID NOS: 3-14). As stated in the Declaration of Dr. Hancock, a non-inventor who is considered an expert in the art of antimicrobial peptides, those in the art understand that dermaseptin cationic peptides are a family of antimicrobial peptides originally isolated from arboreal frogs that are about 27-34 amino acids in length. Although dermaseptin was first isolated from *Phyllomedusa*, dermaseptins have been isolated from other organisms, such as *Pachymedusa* and *Agalychnis* (see page 7, lines 3-21). New members of the dermaseptin family are identified based on their sequence similarity to known dermaseptin sequences.

In view of the dermaseptin definition and sequences provided in the specification, and the statements made in Dr. Hancock’s §1.132 declaration, Applicants request that the 35 U.S.C. §112, second paragraph rejection be withdrawn.

35 U.S.C. §112, first paragraph

Claims 1-9 and 19-20 were rejected under 35 U.S.C. §112, first paragraph on the ground that the claims do not comply with the written description requirement and as not enabled. Applicants respectfully disagree and request reconsideration.

Sufficient written description for dermaseptin sequences is provided in the specification, and in the sequence listing. The specification, sequence listing, and the knowledge in the art, reasonably convey to one skilled in the antimicrobial peptide art that the inventors had possession of the claimed invention. The term “dermaseptin” as used throughout the specification is understood by those skilled in the art (see §1.132 Declaration signed by Dr. Hancock). As discussed above, several dermaseptin nucleic acid and protein sequences are known. In addition, new dermaseptin sequences are being identified based on their sequence similarity to known dermaseptin sequences. Applicants are not claiming dermaseptin sequences per se, but rather are claiming plants incorporating such

sequences to confer disease resistance. Since the inventors have generated transgenic plants that express dermaseptin peptides which confer disease resistance to plants, and have provided 12 different dermaseptin peptides (SEQ ID NOS: 3-14) with varying amounts of sequence identity to one another, the claims comply with the written description requirement.

The specification as written is enabled for microbial-resistant transgenic plants comprising dermaseptin molecules. For example, page 7, lines 3-21 teaches that known dermaseptin molecules have been isolated from several different organisms. In addition, the sequence listing provides 12 different dermaseptin peptides (SEQ ID NOS: 3-14). The specification also teaches how to make vectors containing dermaseptin, how to use such vectors to make transgenic plants, and how to screen transgenic plants for resistance to disease (see pages 29-34). In addition, such molecular biology techniques are well known in the art. Therefore, since the Applicants have enabled at least 12 different dermaseptin peptides with varying amounts of sequence identity to one another, and methods of making transgenic plants are well known in the art, the specification provides sufficient enablement for claims directed to microbial-resistant transgenic plants comprising dermaseptin.

Therefore, the claims satisfy the written description and enablement requirements, and the 35 U.S.C. §112, first paragraph rejections should be withdrawn.

35 U.S.C. §103(a)

Claims 1-6, 8, 9, 12, 14, and 16-20 were rejected under 35 U.S.C. §103(a) as obvious in view of Scheffler *et al.* (EP 0552 559 A2) and Strahilevitz *et al.* (*Biochem.* 33:10951-60, 1994) and Steinberg *et al.* (U.S. Patent No. 6,025,326). Applicants respectfully disagree and request reconsideration.

Enclosed is a § 1.132 Declaration signed by Dr. Misra stating that use of dermaseptin to confer broad disease resistance to plants was not obvious, due to the teachings at the time the invention was made. For example, as noted on page 8 of the present Office action, Florack *et al.* (*Transgenic Res.* 4:132-41, 1995) teach that expression of a cecropin B peptide did not lead to the predicted resistance in plants. Instead, the cationic peptide was rapidly degraded. Similarly, Hightower *et al.* (*Plant Cell Rep.* 13:295-9, 1994) were unable to confer disease resistance to tobacco plants transformed with cecropin B. In addition, Pang *et al.* (*Gene* 116:165-72, 1992) observed that scorpion insectotoxin was not properly processed in tobacco plants, and did not provide the plants with additional disease protection. Based on these teachings, those working in the art (including the

present inventors) did not expect that cationic peptides (such as dermaseptin) could be expressed in plants at levels that would confer disease resistance.

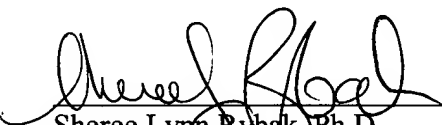
Additionally, based on the teachings at the time the invention was made, it was not obvious that dermaseptin would work against a broad spectrum of plant pathogens. For example, although Scheffler *et al.* (EP 0 552 559) disclose transgenic plants that include magainin, this application only discloses that magainin provides disease resistance to particular bacteria. That cationic peptides could be used to provide protection against fungi was not disclosed or suggested. In contrast, the inventors have found that dermaseptin can be expressed to provide protection against a large variety of pathogens, such as bacteria, fungi (including *Phytophthora infestans* (late blight)) and viruses. In addition, the present inventors have found that such disease protection can be achieved while expressing low-levels of dermaseptin that are not toxic to the plant.

It was not obvious that dermaseptin could be used to confer disease resistance to plants, and the 35 U.S.C. §103(a) rejection should be withdrawn.

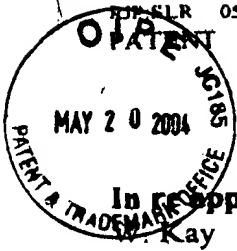
If any matters remain before a Notice of Allowance is issued, the Examiner is invited to telephone the undersigned.

Respectfully submitted,

KLARQUIST SPARKMAN, LLP

By 
Sheree Lynn Rybak, Ph.D.
Registration No. 47,913

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Santosh Misra and William
W. Kay

Application No. 09/936,885

Filed: September 17, 2001

Confirmation No. 2898

For: TRANSGENIC PLANTS THAT ARE
RESISTANT TO A BROAD SPECTRUM
OF PATHOGENS

Examiner: David H. Kruse

Art Unit: 1638

Attorney Reference No. 7013-60993-01

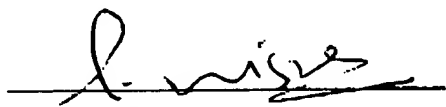
DECLARATION UNDER § 1.132

1. I, Santosh Misra, Ph.D., am a co-inventor named in the above-referenced patent application.
2. I have read and understand the above-referenced patent application, including the pending claims, and the Office action dated February 17, 2004.
3. It is my understanding that in the Office action of February 17, 2004, claims 1-6, 8, 9, 12, 14, and 16-20 were rejected under 35 U.S.C. §103(a) as obvious in view of Scheffler *et al.* (EP 0552 559 A2) and Strahilevitz *et al.* (*Biochem.* 33:10951-60, 1994) and Steinberg *et al.* (U.S. Patent No. 6,025,326). However, it was not obvious to me and my co-inventor Dr. William Kay, that dermaseptin peptides could be used to confer broad disease resistance to plants.
4. At the time the invention was made, there was a significant amount of failure by others in the field. Although several different groups proposed expressing cationic peptides in plants to confer microbial resistance, many were not successful. For example, many journal articles published at the time of the invention disclosed that expression of cationic peptides in plants did not confer microbial resistance. Florack *et al.* (*Transgenic Res.* 4:132-41, 1995) noted that expression cecropin B did not lead to the predicted disease resistance in plants. Instead, the

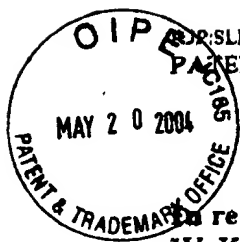
cecropin peptide was rapidly degraded in the plant. Similarly, Hightower *et al.* (*Plant Cell Rep.* 13:295-9, 1994) were unable to confer disease resistance to tobacco plants transformed with cecropin B. Studies using the scorpion insectotoxin indicated that the peptide was not properly processed in tobacco plants, and as a result did not provide the plants with additional disease protection (Pang *et al.*, *Gene* 116:165-72, 1992). Based on these teachings, I did not expect that dermaseptin could be expressed in plants at levels that would confer disease resistance. In addition, there was concern that the amount of dermaseptin that would needed to confer disease resistance would be toxic to the plants. Surprisingly, we found that disease protection was achieved while expressing non-toxic-levels of dermaseptin.

5. It was also not obvious that dermaseptin would be effective against a broad spectrum of plant pathogens. Although some groups were able to confer bacterial resistance by using magainin, that a single cationic peptide could be use to confer resistance to many microbes including yeast, fungi, and bacteria was not obvious. For example, Scheffler *et al.* (EP 0 552 559) only discloses that magainin provides disease resistance to particular bacteria. That cationic peptides could be used to provide protection against fungi was not specifically disclosed or suggested. Surprisingly, we have found that low-levels of dermaseptin can be expressed in plants to confer resistance to bacteria, fungi, and viruses.

6. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.


Santosh Misra, Ph.D.

15/5/04
Date



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PATENT

Attorney Reference Number 7013-60993-01
Application Number 09/936,885

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

**In re application of: Santosh Misra and William
W. Kay**

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RESISTANT TO A BROAD SPECTRUM
OF PATHOGENS**

Examiner: David H. Kruse

Art Unit: 1638

Attorney Reference No. 7013-60993-01

DECLARATION UNDER 1.132

1. I, Robert E.W. Hancock, Ph.D., am an expert in the field of antimicrobial peptides. I hold a Ph.D. from Adelaide. I am currently a Professor in the Department of Microbiology and Immunology at the University of British Columbia (UBC) in Vancouver, British Columbia, Canada, the Director, Centre for Microbial Diseases and Immunity Research at UBC, and the Canada Research Chair in Microbiology/Genomics and Health cluster at UBC. I presently hold 16 issued patents in the field of cationic peptides, and have over 300 publications. A copy of my Curriculum Vitae is attached (Exhibit A).

2. It is my understanding that some of the claims of the above-referenced patent application were rejected as indefinite, on the ground that the term "dermasseptin cationic peptide" is unclear. It is also my understanding that the position of the United States Patent and Trademark Office (PTO) is that those skilled in the art, such as myself, would not know what the term "dermasseptin cationic peptide" referred to.

3. As one skilled in the art of cationic peptides, I declare that those skilled in the art understand what is meant by the term "dermasseptin cationic peptide." Dermaseptin cationic peptides are a family of antimicrobial peptides originally isolated from arboreal frogs that are about 27-34 amino acids in length. Dermaseptins share properties with other short alpha-helical peptides in their ability to be water soluble and interact with phospholipid membranes. However, dermasseptin peptides are distinguished from other alpha-helical cationic peptides (such as magainins and cecropins) both structurally and functionally.

Those skilled in the art of antimicrobial cationic peptides infer structure and function based on the similarities of the sequences.

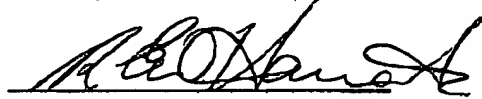
4. Dermaseptin peptides are structurally and functionally different from other cationic peptides. For example, the cecropins, magainins, and dermaseptins vary considerably in chain length, hydrophobicity, and overall distribution of charges. These structural differences lead to functional differences between members of the class of alpha-helical cationic peptides. In addition, because there is no significant sequence homology between dermaseptins and other members of the alpha-helical cationic peptide family, the structure and function of dermaseptins differs. In fact, sequence alignments of dermaseptin molecules with other alpha-helical cationic peptides reveals very low identity. For example, when the dermaseptin amino acid sequence DVLKKIGTVALHAGKAALGAVADTISQ from *Phyllomedusa bicolor* is aligned to the magainin 1 amino acid sequence GIGKFLHSAGKFGKAFVGEIMKS from *X. laevis* only three consecutive amino acids align. Similarly, when the dermaseptin amino acid sequence DVLKKIGTVALHAGKAALGAVADTISQ from *Phyllomedusa bicolor* is aligned to the cecropin amino acid sequence GWLKKIGKKIERVGGQHTRDATIQTIAVAQQAANVAATARG from *Musca domestica* only five consecutive amino acids align. Due to this low level of sequence alignment, those in the art recognize that the structure and function of dermaseptin is distinguishable from those of magainin or cecropin.

5. Those skilled in the art would conclude that a sequence that shared a high amount of sequence alignment with a known dermaseptin sequence would be a member of the dermaseptin family. For example, 22 of the amino acids from the the dermaseptin amino acid sequence DVLKKIGTVALHAGKAALGAVADTISQ from *Phyllomedusa bicolor* align with the dermaseptin amino acid sequence TMLKKLGTMALHAGKAALGAAADTISQGTQ from *Phyllomedusa sauvagei*. In addition, even the amino acids that do not align are conservative substitutions. Due to this high level of sequence alignment, those in the art can identify other dermaseptin molecules, and distinguish them from other alpha-helical cationic peptides.

6. The functions of members of the family of cationic peptides include the ability to kill gram positive bacteria, gram negative bacteria, fungi, viruses, nematodes, helminths, and cancer cells. However, each family member has its own unique combination of abilities, although some functions are shared with other family members. For example, dermaseptins have a broader spectrum of antimicrobial abilities than other antimicrobial peptides. Dermaseptin irreversibly inhibits growth of pathogenic fungi, and can also inhibit the growth of bacteria, yeast, viruses, and protozoa. Another difference between dermaseptins and

other cationic peptides is their inability to lyse erythrocytes. Melittin, pardaxin, magainin, and cecropins all have the ability to lyse erythrocytes.

7. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.


Robert E.W. Hancock, Ph.D.

May 14/2004
Date



Curriculum Vitae

Robert Ernest William HANCOCK, OC, FRSC, FAAM, PhD

EMPLOYMENT: Professor, Microbiology & Immunology, University of British Columbia;
Director, Centre for Microbial Diseases and Immunity Research (CMDR);
Canada Research Chair in Microbiology

EDUCATION: B.Sc. (Hons) Microbiology, University of Adelaide, 1971;
Ph.D. Microbiology, University of Adelaide, 1975

APPOINTMENTS

1975-77 Alexander von Humboldt Stipendiat, University Tubingen, Germany
1977-78 Research Bacteriologist I, University of California, Berkeley
1978-83 Assistant Professor, Microbiology, University of British Columbia
1983-86 Associate Professor with tenure, Microbiology, University of British Columbia
1983- Associate Member, Pediatrics, University of British Columbia
1984-85 Vice President, North West Branch, American Society for Microbiology
1985-86 President, North West Branch, American Society for Microbiology
1986- Professor, Microbiology, University of British Columbia
1987-93 Medical Scientific Advisory Cte, Canadian Cystic Fibrosis Foundation, Chair, 90-93.
1989-96 Founding Scientific Director, Canadian Bacterial Diseases Network
1994 WHO Committee on Antimicrobial Resistance and Surveillance
1997- Director, UBC Centre for Microbial Diseases and Host Defence Research
1998-2002 Chair, PseudoCAP (*Pseudomonas aeruginosa* community genome annotation project)
2000 MRC CIHR Institute Simulation committee.
2000 Genome BC implementation committee.
2001-8 Canada Research Chair in Microbiology/Genomics and Health cluster at UBC.
2001 Officer of the Order of Canada
2001-2 President and Co-Founder, Inimex Pharmaceuticals Inc
2002 Fellow, American Academy of Microbiology
2002-5 Co-Director, Functional Pathogenomics of Mucosal Immunity Program

AWARDS AND DISTINCTIONS

Major

- Zellers Senior Scientist award of the Canadian Cystic Fibrosis Foundation, 2004.
- Aventis Pharmaceuticals Award, 2003 (World's top prize for antimicrobial research from American Society of Microbiology).
- Fellow of the American Academy of Microbiology, 2002.
- Jubilee Medal (Commemorative Medal for 50th anniversary of Queen Elizabeth II's reign), 2002.
- Officer of the Order of Canada, 2001. Innovation and Achievement Award, BC Biotech, 2001.
- Canada Research Chair in Microbiology/Genomics and Health, 2001-2008.
- Jacob Biely Faculty Research Prize, 2000 (Leading research prize at UBC).
- Medical Research Council of Canada/CIHR Distinguished Scientist Award, 1995-00.
- Fellow of the Royal Society of Canada, 1994.
- 125th Anniversary of Canada Silver Medal, 1993 for service (to Canadian Cystic Fibrosis Fdn).
- Canadian Society of Microbiologists/New England Biolabs Lecturer, 1992.
- Founding Scientific Director, Canadian Bacterial Diseases Network of Centres of Excellence, 1989-96.
- Canadian Society of Microbiologists Award, 1987 (For outstanding contributions).



Others

- Interview article about career to date in Lancet Infectious Diseases 3: 736-739; 2003, entitled "Robert E W Hancock – boosting innate immunity to combat infection"
- Listed on ISI Highly Cited Authors in Microbiology at hcr3.isiknowledge.com/home.cgi, ISI author publication number A1065-2002-Z; 20 papers are cited 111 to 569 times.
- Honorary Member, International Golden Key Society, 2002-3.
- UBC Excellence in Research/ Vancouver Institute Lecture, March 9, 2002.
- Featured interview on HMS Beagle, 2000, at www.biomednet.com/hmsbeagle/71/notes/biofeed.
- UBC Science Undergraduate Society Teaching Excellence Award, 1999-2000.
- Featured in Medical Research Council Performance Report to Parliament, March 1999, pp. 19-20: "International calibre health research. Progress in the search for more effective antibiotics".
- Featured in Lifelines, Lancet, May 29, 1998
- UBC Faculty of Science Lecturer, 1992.
- Canadian Who's Who, 1990-04.
- UBC Killam Research Prize, 1988.
- UBC Izaak Walton Killam Memorial Senior Fellowship, 1986-87.
- Foundation for Microbiology lecturer of the American Society for Microbiology, 1985-86.
- Alexander von Humboldt Scholarship for research in West Germany, 1975-77.

SCHOLARLY AND PROFESSIONAL ACTIVITIES

Current Research interests:

Cationic Antimicrobial (Host Defence) Peptides: Mechanism of Action, Structure:Function relationships; Peptide: membrane interactions; Structure of antimicrobial peptides; Aerosol delivery of peptides as a potential therapeutic strategy for cystic fibrosis; Use in transgenic plants.

Cationic Host Defence Peptides: Involvement of peptides in innate immunity in humans, and mice; Microarray studies of peptide interaction with human, mouse, fungal and bacterial cells; Mechanism of interaction of peptides with human epithelial, monocyte and macrophage-like cells; Anti-endotoxic activity of antimicrobial peptides.

Biotechnology: Rational antimicrobial peptide design for improved uptake; Recombinant synthesis of peptide antibiotics; Use of peptides in food preservation; Design of peptides for boosting Innate Immunity and overcoming harmful inflammation.

Outer membranes of Gram negative bacteria: especially *Pseudomonas aeruginosa*. Molecular genetics of outer membrane proteins; outer membrane proteins and porins of other gram negative bacteria; Interactions of outer membrane proteins with host cells, role of the outer membrane in pathogenesis.

Antibiotics: Antibiotics and outer membrane permeability; mechanisms of antibiotic resistance and efflux; Adaptive and mutational resistance to antibiotics

Genomic studies of Pseudomonas aeruginosa: Pathogenomics, functional genomics and informatics; Microarray studies; Construction of *lux*-fusion knockout libraries.

Research or equivalent grants

Research Granting Agencies: Canadian Bacterial Diseases Network; Medical Research Council of Canada (now CIHR); Networks of Centres of Excellence; Canadian Cystic Fibrosis Foundation; CCFF SPARx Program, US CF Foundation, NSERC, Genome Canada.

Research Grant: Funding (Individual totals) 1978-2004, \$15,809,165. Co-funded \$306,660.

Group grants: (As principal applicant and program leader) \$61,031,414.

Equipment Grants: Funding Totals 1978-2004, \$1,192,379. In addition, I participated as an applicant in several joint equipment grants to CFI (totalling more than \$180,000,000).

Research Contracts: Funding Totals 1982-2004, \$1,330,193.

Invited Major Meeting Presentations

(Last 2 years of total 147; More than 200 talks at Universities and Companies not included)

1. UBC Excellence in Research/ Vancouver Institute Lecture, Vancouver, March 9, 2002.
2. BC Biotech Alliance Breakfast lecture, Vancouver, March 13, 2002.
3. CBDN/CMCI AGM 2002, Saskatoon, Canada, June 20-22, 2002.
4. AstraZeneca Symposium on Bacterial Permeability and Efflux, Boston, MA, Nov.8, 2002
5. Biofuture 2002, Vancouver, BC, Nov.21-22, 2002. Genomics session Chair & speaker.
6. Consumer Specialty Products Assn, Annual Meeting, Ft. Lauderdale, Dec.10, 2002.
7. 3rd ASM & TIGR Conference on Microbial Genomes, New Orleans, LA, Jan 29-Feb 1, 2003.
8. Genome BC Genomics Forum, Vancouver, March 27th, 2003.
9. 4th GRC on Antimicrobial Peptides, Barga, Italy, April 27-30, 2003.
10. Pore forming toxins and Maxi-channels. GRTM 21st Symposium, Montreal, May 26-28, 2003.
11. Bovine Genomics Workshop, Montreal, Quebec, June 17-19, 2003.
12. Bio2003 Annual Convention, Washington Convention Center, DC, June 22-25, 2003
13. 2003 International Pseudomonas Mtg, Keynote speaker, Quebec City, September 8, 2003.
14. ICAAC. Aventis Award Lecture, Chicago September 15, 2003.
15. Ann Mtg of Austrian Soc Biochemistry & Molecular Biology, Graz, Austria, Sept. 21-25, 2003.
16. Commercialise 2003. Melbourne, Australia, Nov 18, 2003.
17. Building Biotech Symp., UBC Student Biotechnology Network and BC Biotech, Feb. 26, 2004.
18. Genomics and the Science of Life Forum, Genome BC, March 26, 2004.
19. FDA Proteins and Peptides Workshop, U. Maryland, April 26, 2004.

Conference Organizer. (Last 5 years of total 17 meetings organized)

Conference Committee: North American Cystic Fibrosis Meeting, Montreal, October 15-18, 1998

Vice Chair: 2nd Gordon Conference on Antimicrobial Peptides, April 25-30, 1999

Organizing Committee: Wall Antibiotic Resistance Meeting, April 23-25, 1999

Co-Chair: Gordon Conference on Antimicrobial peptides, Ventura, Ca, March 2001

Organizer: meeting re establishing a Canadian Infection and Immunity Inst., Ottawa, Jan 14, 2000

Co-organizer: meeting re establishing a Canadian Food and Water Safety Network, June 2-4, 2000

Co-organizer: Broken Arrow mtg of the Canadian Cystic Fibrosis Foundn, Toronto, Sept. 7-9, 2001

Chair and Co-founder: 1st Gordon Conference on Multi Drug Efflux Systems, 2003.

Graduate Students Graduated

Thalia I. Nicas, Ph.D. (1978-82); Barbara Angus, Ph.D. (1980-86); Lucy Mutharia, Ph.D. (1980-84); R. Keith Poole, Ph.D. (1981-86); Bernadette Loh, M.Sc. (1981-84); Janet Sawyer, M.Sc. (1985-87); Wendy Woodruff, Ph.D. (1983-88); Angus Bell, Ph.D. (1984-89); Janet Kluftinger, Ph.D. (1984-89); Nancy Martin, Ph.D. (1985-92); Catherine Ullstrom, M.Sc. (1986-90); Kevin Piers, Ph.D. (1987-93); Eileen Rawling, Ph.D. (1988-95); Renee Finnen, M.Sc. (1989-91); Michelle Young, M.Sc. (1990-92); Rebecca Wong, Ph.D. (1990-95); Anand Sukhan, Ph.D. (1991-96); Xiaowen Liao, Ph.D. (1991-96); Hongjin Huang, Ph.D. (1991-95); Maurice Exner, Ph.D. (1991-97); Manhong Wu, Ph.D. (1993-98); Matthew McCusker, M.Sc. (1996-98); Agnes Kwasnicka, M.Sc. (1997-99); Monisha Scott, M.Sc. (1996-98); Kendy Wong, Ph.D. (1994-2001); Carol Friedrich, Ph.D. (1995-2001); Aleks Partzykat, Ph.D. (1996-2001); Monisha Scott, Ph.D. (1998-2002); Jim Jo, M.Sc. (1999-2002).

SERVICE TO THE COMMUNITY

Public Relations Experience

- Especially in my duties as the Scientific Director of the Canadian Bacterial Diseases Network and the Director of CMDR, I have talked to numerous reporters in print, radio and television, appeared on many radio programs including CBC local and national (and Quirks and Quarks twice), CKNW, etc, on television on CBC, CTV, BCTV, King TV, French CBC, Discovery.CA, etc. Appeared in print in the Vancouver Sun (including 3 front page articles), Fortune Magazine, Globe and Mail, Province, Omni, MacLean's, Time, Equinox, Ottawa Citizen, Toronto Star, Edmonton Journal, Calgary Herald,

Montreal Gazette, Canadian Biotech News, Winnipeg Free Press, Bioworld, etc.

- As Chair of the MSAC of the Canadian Cystic Fibrosis Foundation was responsible for reporting to parents and patients about research on cystic fibrosis.
- Participated in 2 large-scale TV productions "Plants that heal" on Discovery channel (replayed throughout the world) and "Antibiotic Resistance" on CBC Prime time (replayed 4 times to date).

Memberships on scholarly committees.

- President, Northwest Branch, American Society for Microbiology, 1985-86.
- Vaccine Evaluation Centre, Advisory Board, 1988-92.
- MRC Grants committee for Microbiology and Infectious Diseases 1982-84.
- Canadian Cystic Fibrosis Foundation Grants Committee, 1987-90.
- Member, Alberta Heritage Found for Med Res Scholarship Applications Advisory Cte, 1989-90.
- Canadian Society of Microbiologists, CSM Awards Committee, 1994-7; Chair, 1997.
- Coordinator of the PseudoCAP (*Pseudomonas aeruginosa* genome community annotation) project with 60 International volunteers, 1997-2000; Co-coordinator with Fiona Brinkman since 2000.
- Fellowship Review Cte, Life Sciences Div., Acad. III, Royal Society of Canada, 1998-2001
- Coordinator of a proposal to create a Canadian Institute for Infectious Diseases and Immunity within CIHR, 1999-2000.
- Member, Executive Group of the Multi-Centre Network for Viral Hepatitis, 2000.
- Member, Executive to coordinate Canadian Food Microbiology activities, 2000-2001.
- UBC CIHR transition committee, 2000
- Vancouver Hospitals HSC Microbial Pathogenesis Review Committee, 2000-2.
- Canada Research Chair College of Reviewers, 2000-3
- Panel member/presenter Mike Smith Foundn for Health Research retreat, Vancouver Feb 1/02.
- Michael Smith Foundation for Health Research, Scientific Advisory Board, 2001-3

Selected Editorial Boards.

Editorial Board, Journal of Bacteriology, 1982-90.

Editorial Board, Infection and Immunity, 1986-89.

Editorial Board, Antimicrobial Agents and Chemotherapy, 1987-05.

International Advisory Board, Current Microbiology and Infection, 1996 -
Drug Resistance Updates, 1997-

Editorial Board, Current Opinion in Anti-infective Drugs, 1998-

Reviewer

Review about 80 manuscripts, grants and reviews per year for Nature, Nature Biotechnology, J. Bacteriology, Infection & Immunity, Antimicrobial Agents & Chemotherapy, Peptides, J. Biological Chemistry, J. Peptide Research, J. Membrane Biology, J. Antimicrobial Chemotherapy, FEBS Letters, Proc Natl Acad Sci., Microbiology, Molecular Microbiology, CIHR, NSERC, Canadian Cystic Fibrosis Foundation, US Cystic Fibrosis Foundation etc.

Industrial Experience.

Micrologix Biotech Inc. This TSE-listed company arose from the research of my laboratory. It is capitalized at around \$80,000,000, has more than 50 employees and is in 2 sets of clinical trials, one phase III (recently completed with success in secondary but not primary objectives for prevention of catheter associated infections), and one phase IIb completed for acne.

CBDN. As Scientific Director of CBDN, I participated in the outlicensing of more than 2 dozen technologies and in the formation of 6 companies. I was an early participant, advisor and SAB member in 3 other companies, *Helix Biomedix*, and *Versicor*.

Inimex Pharmaceuticals Inc. President and Co-founder with Brett Finlay

Consultant

Centocor Corporation, Philadelphia, Pennsylvania, 1983-86; Bristol-Myers-Squibb, Ltd., Syracuse, New York, 1984-91; Oncogen, Seattle, WA, 1988-91; Genta Inc., San Diego, 1993-95; Cubist Pharmaceuticals, 1994; Micrologix Biotech Inc, Vancouver, BC, 1994-98; Affymax Inc., Santa Clara, CA., 1995; Gruppo Lepetit (Marion Merrill Dow), Geranzano, Italy, 1995; Vicuron, San Francisco, CA, 1996- (named Versicor from 1996-2001); Canadian Department of National Defence, Ottawa, 1996-7; Proctor-Gamble, Connecticut, 1997; Canadian Inovatech, Abbotsford, BC, 1997-2000; Pathogenesis, Seattle, 1998; Becton Dickinson, Raleigh Durham, 1998; Geltex, Boston, 1998-9; Synphar Inc, Edmonton, 1998-2000; National Research Council, 1999-2000; Smart & Biggar/Astra, 2000; Helix Biomedix, 2001-; Ortho-McNeil Pharmaceuticals, 2001; Symyx, 2002.

Boards

Board of Directors, Micrologix Biotech Inc., Vancouver, 1992-95; Scientific Advisory Board, Chair, Micrologix Biotech Inc., Vancouver, 1995-98; Scientific Advisory Board, Infectious Diseases Biomedical Inc., Vancouver, 1992-95; Board of Directors, Canadian Foundation for Infectious Diseases, 1994-96; Board of Directors, Chair, David Elford Holding Company, 1995-7. Board of Directors, Novadex Inc., B.C. 1995-96; Scientific Advisory Board, Versicor, San Francisco, 1995-; Advisory Board, Polydex Inc, New York, 1996-8; Scientific Advisory Board, Welichem, Vancouver, 1996-; Chair, Board of Directors, David Elford Forest Management Ltd., 1997-02; Scientific Advisory Board, Helix Biomedix, Seattle, 2000-; President, Inimex Pharmaceuticals, Vancouver, 2001-02; Board of Directors, Inimex Pharmaceuticals, Vancouver, 2001-.

Publications Record

NB. Listed on ISI Highly Cited Authors in Microbiology at hcr3.isiknowledge.com/home.cgi, ISI author publication number A1065-2002-Z; 20 papers are cited 111 to 569 times.

Robert Ernest William HANCOCK

Date: May/2004

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1. Skurray, R.A., R.E.W. Hancock, and P. Reeves. 1974. Con mutants: class of mutants in *Escherichia coli* K-12 lacking a major cell wall protein and defective in conjugation and adsorption of a bacteriophage. *J. Bacteriol.* 119:726-735.
2. Hancock, R.E.W., and P. Reeves. 1975. Bacteriophage resistance in *Escherichia coli* K-12: General pattern of resistance. *J. Bacteriol.* 121:983-993.
3. Hancock, R.E.W., J.K. Davies, and P. Reeves. 1976. Cross resistance between bacteriophages and colicins in *Escherichia coli* K-12. *J. Bacteriol.* 126:1347-1350.
4. Hancock, R.E.W. and P. Reeves. 1976. Lipopolysaccharide-deficient, bacteriophage-resistant mutants of *Escherichia coli* K-12. *J. Bacteriol.* 127:98-108.
5. Hancock, R.E.W., and V. Braun. 1976. Nature of the energy requirement for the irreversible adsorption of bacteriophages T1 and ϕ 80 to *Escherichia coli*. *J. Bacteriol.* 12:409-415.
6. Hancock, R.E.W., and V. Braun. 1976. The colicin I receptor of *Escherichia coli* K-12 has a role in enterochelin-mediated iron transport. *FEBS Lett.* 65:208-210.
7. Braun, V., R.E.W. Hancock, K. Hantke, and A. Hartmann. 1976. Functional organization of the outer membrane of *Escherichia coli*. Phage and colicin receptors as components of iron uptake systems. *J. Supramolecular Structure* 5:37-58.
8. Hancock, R.E.W., K. Hantke, and V. Braun. 1976. Iron transport in *Escherichia coli* K-12: Involvement of the colicin B receptor and of a citrate-inducible protein. *J. Bacteriol.* 127:1370-1375.
9. Hancock, R.E.W., K. Hantke, and V. Braun. 1977. Iron transport in *Escherichia coli* K-12: 2,3-dihydroxybenzoate-promoted iron uptake. *Arch. Microbiol.* 114:231-239.
10. Hancock, R.E.W., and H. Nikaido. 1978. Outer membrane of Gram negative bacteria. XIX Isolation from *Pseudomonas aeruginosa* PAO1 and use in reconstitution and definition of the permeability barrier. *J. Bacteriol.* 136:381-390.

11. Hancock, R.E.W., and G.M. Decad and H. Nikaido. 1979. Identification of the protein producing transmembrane diffusion pores in the outer membrane of *Pseudomonas aeruginosa* PA01. *Biochim. Biophys. Acta.* 554:323-331.
12. Hancock, R.E.W., and A.M. Carey. 1979. Outer membrane of *Pseudomonas aeruginosa*. Heat-and 2-mercaptoethanol-modifiable proteins. *J. Bacteriol.* 140:902-910.
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14. Hancock, R.E.W., and A.M. Carey. 1980. Protein D1 - a glucose-inducible, pore-forming protein from the outer membrane of *Pseudomonas aeruginosa*. *FEMS Microbiol. Letters* 8:105-109.
15. Nicas, T.I., and R.E.W. Hancock. 1980. Outer membrane protein H1 of *Pseudomonas aeruginosa*: Involvement in adaptive and mutational resistance to ethylenediamine tetraacetate, polymyxin B and gentamicin. *J. Bacteriol.* 143:872-878.
16. Hancock, R.E.W., R.T. Irvin, J.W. Costerton, and A.M. Carey. 1981. *Pseudomonas aeruginosa* outer membrane: peptidoglycan associated proteins. *J. Bacteriol.* 145:628-631.
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23. Mutharia, L.M., T. I. Nicas, and R.E.W. Hancock. 1982. Outer membrane proteins of *Pseudomonas aeruginosa* serotype strains. *J. Infect. Dis.* 146:770-779.
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16. Antimicrobial peptides and methods of use thereof. R.E.W.Hancock and L.Zhang. **European patent 1,294,745 issued March 26, 2002.**



TRANSGENIC PLANTS THAT ARE RESISTANT TO A BROAD SPECTRUM OF PATHOGENS

ABSTRACT

5 Transgenic plants that express dermaseptin and/or temporin peptides are disclosed. In certain embodiments, these plants have enhanced, broad-spectrum pathogen resistance and are useful as agricultural or horticultural crops. In other embodiments, the plants are used to produce large quantities of the dermaseptin and/or temporin peptides.